

U.S.S.N. 09/096,648
HADLACZKY *et al.*
PRELIMINARY AMENDMENT

64 82. (Amended) A method of producing a transgenic embryo, comprising:
introducing a satellite artificial chromosome into a cell, wherein the cell is
capable in culture of developing into an embryo; and
culturing the cell under conditions whereby it develops into an embryo.

83. (Amended) The method of claim 82, wherein the cell comprises a
fertilized oocyte, an ovum, a fertilized ovum or a zygote.

65 98. (Twice Amended) A method for producing a transgenic non-human
mammal, comprising:

introducing a fertilized oocyte comprising a satellite artificial chromosome
into a female non-human mammal; and

allowing the resulting embryo to develop into a transgenic non-human
mammal comprising a satellite artificial chromosome.

REMARKS

A check for the fees for a three month extension of time and a RCE
accompanies this response. Any fees that may be due in connection with filing
this paper or with this application during its entire pendency may be charged to
Deposit Account No. 50-1213. If a Petition for extension of time is required, this
paper is to be considered such Petition, and any fee charged to Deposit Account
No. 50-1213.

Claims 32, 35, 38, 39, 65, 67, 82, 83, 97-100 and 106-110 are presently
pending in this application. Claims 98 and 99 are deemed allowable. Claims 33,
34, 36, 37, 43, 44, 59, 60, 71-74, 84-86, 88, 89 and 93-96 are cancelled
without prejudice or disclaimer. Claims 32, 82, 83 and 98 are amended in order to
more particularly point out and distinctly claim the subject matter that applicant
regards as the invention. No amendments have been made to obviate prior art and
no new matter has been introduced. Claims 106-110, which are provided in
accord with suggestions by the Examiner (see, page 7 of the Office Action), are
added.

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The amendments to claims 32, 67, 82, 83 and 98 correct minor typographic and dependency errors. The amendments to claims 32, 67, 82, 83 and 98 find basis in the specification and claims as originally filed. New claim 106 finds basis on page 34, lines 15-25 and in original claim 65. New claim 107 finds basis on page 44, lines 17-22 and in original claim 67. New claim 108 finds basis in the specification on page 34, lines 15-25 and in original claim 65. New claim 109 finds basis in the specification on page 8, line 28, through page 9, line 2 and page 34, lines 25-31. New claim 110 finds basis in the specification on page 9, lines 2-10, page 34, lines 15-25, and page 109, lines 13-23.

These amendments are intended to clarify the subject matter encompassed by the claims. Therefore, since the amendments change the form, not the substance of the claimed subject matter, no new matter has been added.

A marked-up copy of the amended claims, as per 37 C.F.R. §1.121, is attached to this response. Accordingly, entry of the amendments to the claims is respectfully requested.

THE REJECTION OF CLAIMS 32-39, 43, 44, 59, 60, 65, 67, 71-74, 82-89, 93-97 and 100 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 32-39, 43, 44, 59, 60, 65, 67, 71-74, 82-89, 93-97 and 100 under 35 U.S.C. §112, first paragraph, as being broader than the enabling disclosure. In particular the Examiner urges that independent claims 32, 43, 44, 73, 74, 82, 93, 95 and 96, recite the term "cell(s)" and read broadly on all cells, and it is well known in the art that only particular cells, such as a fertilized ovum, would be capable of developing into an animal. It is further asserted that claims dependent on the recited independent claims are included in the rejection as the claims are not complete and are missing critical steps dependent upon the source cells. The Examiner alleges that although dependent claims do further limit and distinguish particular cells that are sufficient with regard to the enabled scope, the invention as broadly claimed encompasses any type of cell(s), and the introduction of an artificial chromosome into these cell(s) as broadly claimed, would not be sufficient to produce any animal.

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Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks. It is noted, however, that the bases for rejection are rendered moot by cancellation of claims 33, 34, 36, 37, 59, 60, 71-74, 84-86, 88, 89 and 93-96 and are obviated by amendment of claims 32, 82 and 83 to indicate the type of cell capable of development into a transgenic non-human mammal.

The claims and analysis

Claim 32 recites that the cell is one that is capable in the female non-human mammal of developing into an embryo in a female non-human mammal. Claim 35, 38, 39, 65, 67, 100 and 108 are dependent upon claim 32, and thereby incorporate its limitations. Claims among these specify that the cell is a fertilized ovum or a zygote. Hence all of these claims encompass cells that develop in a non-female mammal into a mammal. Further, none of these claims are dependent upon the source of the cells, since claims are directed to the particular cells are those that develop in the female into an embryo. The Examiner states that "it is well known in the art that only particular cells, such as a fertilized ovum," are "capable of developing into an animal."

Claim 82 is directed to a method of producing a transgenic embryo by introducing a SATAC into a cell that is capable of developing into an embryo, and culturing the cells to produce an embryo. Dependent claim 83 specifies that cell is a fertilized oocyte, an ovum, a fertilized ovum or a zygote all of which can develop in culture into an embryo. As above, the claim is directed to use of particular cells that are capable of developing into an embryo in culture.

Claim 97 is directed to:

A method for producing a transgenic non-human mammal, comprising:
introducing an embryo comprising a satellite artificial chromosome
into a female non-human mammal; and
allowing the embryo to develop into a transgenic non-human mammal
comprising a satellite artificial chromosome.

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Claim 97 does not appear to be within the purview of this rejection because it is directed to introduction of an embryo into the non-human mammal. Embryos are capable of development in a female mammal into a mammal.

As pending the independent claims are not directed to "any cell", but specify that the cells develop in the female into an embryo or in culture (claims 82 and 83) into an embryo. The Examiner recognizes that "it is well known in the art that only particular cells" can develop into an animal. With respect to the dependent claims, the specified source cells are those for which additional steps are not required.

As described in the response (mailed February 26, 2002) to the previous Office Action and the response (mailed May 26, 2002) to the previous Advisory Action, a variety of cells may be used in the claimed methods. Exemplary cells for use in the claimed methods are referred to in the application. In addition, in considering the teachings of the specification in combination with transgenic animal production methods known in the art at the time of filing of the instant application, it is clear that one of skill in the art could readily determine a number of cells that may be used in the claimed methods. Numerous books and review articles detailing various procedures for the production of transgenic animals, including the use of source cell(s), such as embryos, oocytes, zygotes, embryonic stem cells, gametes and germline cells were known at the time of filing of the instant application (see, *e.g.*, "Animals with Novel Genes", Maclean (Ed.), Cambridge University Press, 1994; "Transgenic Animal Technology", Pinkert (Ed.), Academic Press, 1994; Capecchi, "Targeted Gene Replacement", *Sci. American* 270(3): 52-59 (1994); Bondioli "Nuclear Transfer in Cattle" *Mol. Reprod. Dev.* 36: 274-275 (1993); Kaufman *et al.* "Handbook of Molecular and Cellular Methods in Biology and Medicine" CRC Press, pp. 357-365 (1995); Fässler *et al.* "Knockout Mice: How to Make Them and Why. The Immunological Approach" *Int. Arch. Allergy Immunol.* 106: 323-334 (1995); Campbell *et al.* (1996) *Nature* 380:64-66; and PCT Application Publication No. WO 95/17500). Therefore, as recognized by

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the Examiner, "it is well known in the art that only particular cells" can develop into an animal and one of skill in the art can combine the teachings of the specification with transgenic animal production methods known in the art at the time of filing and identify what source cell(s) can be used in the production of transgenic embryos and non-human mammals.

Also, since it is known that several source cell(s) are capable of development into an embryo or non-human mammal, it would be unfair and unduly limiting to require applicant to limit these claims to a specific cell source. To do so is contrary to the public policy upon which the U.S. patent laws are based. If Applicant is required to limit the claims only to a fertilized ovum and mouse embryonic stem cells as urged by the Examiner, those of skill in the art could by virtue of the teachings of this application readily practice what is claimed by substituting another source cell such as a fertilized oocyte, a zygote or using an embryo and practice what is disclosed in the application, but avoid infringing such limited claims. To permit that is simply not fair. The instant application exemplifies that the artificial chromosomes as provided therein are convenient and useful vectors for the introduction of heterologous genes into hosts and may be used in any methods that conventional vectors are used and other methods. The specification provides numerous examples of the use of the artificial chromosomes as vectors in a variety of methods, including the generation of transgenic animals (see, *e.g.*, EXAMPLE 14 in the specification). The executed DECLARATION of Perez under 37 C.F.R. §1.132 (mailed January 29, 2001) further demonstrates that it is possible to follow the teachings of the specification to use artificial chromosomes in the generation of transgenic embryos and animals as described in the application. Having done so, it is now routine for others to introduce SATACs into other source cell(s) and produce a transgenic embryo or non-human mammal. Those of skill in the art should not be permitted to make such minor modifications by substitution of a different host and avoid infringing such claims.

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THE REJECTION OF CLAIMS 32-39, 43, 44, 59, 60, 65, 67, 71-74, 82-89, 93-96, and 100 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 32-39, 43, 44, 59, 60, 65, 67, 71-74 and 82-89, 93-97 and 100 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because they are allegedly incomplete in failing to specify steps of the methods. The Examiner alleges that:

it is a huge leap to go from the introduction of an artificial chromosome into a cell to the development of a transgenic mammal. Particularly, as more is required, including essential steps, such as introducing an ES cell or fertilized ovum, for example, transplanting the embryo into a recipient non-human mammal, allowing the embryo to develop to term, and identifying the transgenic non-human mammal whose genome comprises a SATAC.

Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks.

The Examiner states that the claims are incomplete because they are missing critical steps required to go from any cell to one that develops into an embryo or transgenic animal. As pending all claims recite cells that are capable of developing into an embryo in a non-human mammal or recite that an embryo, zygote, ovum or other such cell or cells are introduced, there are no missing critical steps.

Claim 32 recites that the cell is one that is capable in the female non-human mammal of developing into an embryo in a female non-human mammal. Claim 35, 38, 39, 65, 67, 100 and 108 are dependent upon claim 32, and thereby incorporate its limitations. Claims among these specify that the cell is a fertilized ovum or a zygote. Hence all of these claims encompass cells that develop in a non-human female mammal into a mammal.

Claim 82 is directed to a method of producing a transgenic embryo by introducing a SATAC into a cell that is capable of developing into an embryo, and culturing the cells to produce an embryo. Thus, there are no missing critical steps, since all that is required is culturing of the cell. Dependent claim 83

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specifies that cell is a fertilized oocyte, an ovum, a fertilized ovum or a zygote all of which can develop in culture into an embryo.

Claim 97 is directed to:

A method for producing a transgenic non-human mammal, comprising:
introducing an embryo comprising a satellite artificial chromosome
into a female non-human mammal; and
allowing the embryo to develop into a transgenic non-human mammal
comprising a satellite artificial chromosome.

Since an embryo clearly can develop into a mammal, there are no missing steps in claim 97. It appears that claim 97 is outside the purview of this rejection. Claims 109 and 110 are dependent upon claim 97.

* * *

In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By: 

Stephanie L. Seidman
Registration No. 33,779

Attorney Docket 24601-402A
Address all correspondence to:
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 7th Floor
San Diego, California 92122-1246
Telephone: (858) 450-8400
Facsimile: (858) 587-5360
E-mail: sseidman@HEWM.com

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Applicant: HADLACZKY *et al.*

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THEREOF AND METHODS FOR
PREPARING ARTIFICIAL CHROMOSOMES**

Group Art Unit: 1632

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Jonathan Ong
Jonathan Ong

MARKED UP CLAIMS (37 C.F.R. § 1.121)

Please amend claims 32, 65, 82, 83 and 98 as follows:

32. (Amended) A method for producing a transgenic non-human mammal, comprising:

introducing a cell comprising a satellite artificial chromosome into a female non-human mammal, is capable of developing into an embryo in a female non-human mammal; and

allowing the cell to develop into a transgenic non-human mammal comprising a satellite artificial chromosome.

65. (Amended) The method of claim 32, wherein the [animal] cell is a fertilized ovum.

82. (Amended) A method of producing a transgenic embryo, comprising: introducing a satellite artificial chromosome into a cell, wherein the cell is capable in culture of developing into an embryo; and

culturing the cell under conditions whereby it develops into an embryo.

83. (Amended) The method of claim 82, wherein the [cell is an oocyte] cell comprises a fertilized oocyte, an ovum, a fertilized ovum or a zygote.

98. (Twice Amended) A method for producing a transgenic non-human mammal, comprising:

introducing a fertilized oocyte comprising a satellite artificial chromosome into a female non-human mammal; and

allowing the resulting embryo to develop into a transgenic non-human mammal comprising a satellite artificial chromosome.